## Remarks

Claims 25-27 and 42 were examined in the Office Action dated October 9, 1996 and rejected based on (1) 35 USC §112, first paragraph, as nonenabled; (2) 35 USC §112, second paragraph, as indefinite (claim 42); and (3) 35 USC §102, as anticipated.

These rejections are believed to be overcome by the above amendments and are otherwise traversed, as discussed below.

### Overview of the Above Amendments and New Claims

Claims 25-27 have been amended to recite recombinant protein preparations that comprise PDGF A-chain homodimers. The preparations are characterized as being produced in a nonhuman cell such that the preparations are free of other human proteins.

Claims 43-54 have been added. These claims recite preparations and methods of using the PDGF A-chain homodimers of claims 25-27.

Support for the amendments and new claims can be found throughout the specification at, *inter alia*, page 13, lines 9-21 and in the examples. Thus, no new matter has been added to the application by way of the new claims. Applicants submit that any search on the existing claims would have captured subject matter pertaining to the new claims and that these claims, therefore, should properly be examined in the present application.

Claim 42 has been cancelled. Cancellation is not meant to be an acquiescence in any rejections and is made without

prejudice to applicants' right to bring the claims again in a related application.

Finally, the title has been amended to more accurately reflect the claimed invention.

Rejections Under 35 USC §112, First Paragraph

Claims 25-27 were rejected under 35 USC §112, first paragraph. The Action recognizes that the specification is enabling for PDGF A-chain homodimers having the sequences depicted in Figures 1 and 2. However, the Action alleges that analogs of PDGF A-chain homodimers which are substantially homologous and functionally equivalent to the sequences depicted are not enabled. The Action supports the rejection based on reasons presented in Paper No. 5, pages 5-6 and Paper No. 8, pages 2-5. Paper No. 5 argues that no guidance is provided as to where within the protein substitutions and deletions can be made and that it is "highly unlikely that any amino acid within the PDGF A-chain protein could be substituted or deleted" without some alteration of biological function, proper folding, etc. Paper No. 8 reiterates this rejection and asserts that the claims "broadly encompass a significant number of inoperative species" despite the inclusion of the claim terminology "functionally equivalent." However, applicants do not agree with these assertions.

In order to satisfy the enablement requirement of Section 112, the specification need only set forth such information as is sufficient to allow one of ordinary skill in the art to make and use the invention. How such a teaching is accomplished, either by the use of illustrative

examples or by broad terminology, is of no importance since a specification which teaches how to make and use the invention in terms which correspond in scope to the claims must be taken as complying with the first paragraph of §112 unless there is reason to doubt the objective truth of the statements relied upon therein for enabling support (*In re Marzocchi*, 169 USPQ 367 (CCPA 1971)). Indeed, it is well settled that a patent need not teach, and preferably omits, what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81 (Fed. Cir. 1986). Accord, *Paperless Accounting, Inc. v. Bay Area Rapid Transit*, 231 USPQ 649, 653 (Fed. Cir. 1986) ("A patent applicant need not include in the specification that which is already known to and available to the public."). Applicants have certainly complied with these tenets.

In this regard, methods for recombinantly producing the claimed PDGF A-chain homodimers are described in great detail in the specification at, e.g., pages 6-13 and in the Examples. Furthermore, methods for producing modified sequences for PDGF are also described in the specification at, for example, page 11. Additionally, methods for recombinantly preparing peptides having amino acid modifications were known as of the filing date of the application and it was well known, for example, which modifications could reasonably be expected to result in a protein retaining the native properties. For example, it was and is generally accepted that conservative amino acid substitutions are well tolerated. Furthermore, it was and is known that certain amino acids lend themselves to

substitution without substantial changes in the activity of the protein in question.

Additionally, as applicants have previously explained, an analog of a PDGF A-chain homodimer that is "functionally equivalent" intends that the analog has the biological activity of PDGF as measured by the assay described in Example 5 (see page 6, lines 27-31 of the specification). Since applicants have taught how to make PDGF A-chain homodimers and analogs thereof, as well as methods for testing such analogs for biological activity, one of skill in the art could readily make and test a variant PDGF A-chain homodimer without undue experimentation.

Applicants submit that, given the description in the specification, the particular examples, and the level of skill in the art, a skilled artisan could readily practice the claimed invention without undue experimentation. See, e.g., *Utter v. Hiraga*, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988), and *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). The Examiner is reminded that even a large amount of experimentation is permitted under §112, first paragraph, provided it is routine. *Ex parte Jackson*, 217 USPQ 804, 807 (POBA 1982) (a claim is acceptable under §112 even if it requires extensive experimentation, as long as the experimentation is routine).

Furthermore, it is not incumbent on applicants to detail all potential analogs falling within the scope of the claims in order to comply with 35 USC §112, first paragraph. In fact, the CCPA in *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976), cautions against such a burdensome requirement.

With regard to the Action's statement that the

claims "encompass a significant number of inoperative species" such is not a proper basis for rejection. As stated by the court in *In re Sarett*, 140 USPQ 474 (CCPA, 1964):

> "In any event, the mere possibility of inclusion of inoperative substances does not prevent allowance of broad claims. * * * If they are so broad as to be vulnerable, no one but the patentee will suffer from it.
>
> It is certainly not incumbent on an applicant who has made a broad process invention and supported it by an adequately broad disclosure to demonstrate the operativeness of every substance falling within the scope of the broad claims to which he is entitled. ... The function of the claims is to point out the invention and define the scope of the monopoly, not to exclude substances which are possibly of no use in practicing the invention." 140 USPQ at 486 (emphasis in original).

For all of the foregoing reasons, it is submitted that the application complies with the requirements of 35 USC §112, first and second paragraphs and these bases for rejection should be withdrawn.

Rejection Under 35 USC §112, Second Paragraph

Claim 42 was rejected under 35 USC §112, second paragraph, as indefinite. However, this claim has now been cancelled. Hence, this basis for rejection has been rendered moot.

Rejections Under 35 USC §102

The claims were rejected under 35 USC §102(a), as anticipated by Betsholtz et al. *Nature* (1986) 320:695-699 ("Betsholtz") and claims 25-27 were rejected under 35 USC §102(e), as anticipated by U.S. Patent No. 4,889,919, to

Murray ("Murray"). However, applicants submit that they have properly eliminated Betsholtz as a reference and have antedated Murray. In particular, applicants, in the grandparent application, Serial No. 07/574,540 (now issued as U.S. Patent No. 5,219,759), eliminated Betsholtz as a reference by way of a Rule 131 Declaration signed by each of the inventors. A copy of this Declaration is appended hereto and applicants request that it be made of record in the present application. Thus, Betsholtz is not properly citable against the present claims.

The Rule 131 Declaration also serves to antedate Murray. In this regard, the earliest application in the Murray lineage that refers to the PDGF A-chain is U.S. Serial No. 896,485, now issued as U.S. Patent No. 4,766,073. This patent was filed on August 13, 1986, after the Betsholtz article which, as described in the Declaration, is the basis for the present application. Applicants are submitting a copy of the parent to the '073 patent, U.S. Serial No. 705,175, as well as a copy of U.S. Patent No. 4,769,328 (corresponding to the earliest application in the Murray series) for the Examiner's review. Thus, Murray has also been successfully antedated. Accordingly, applicants request withdrawal of the rejections over Betsholtz and Murray.

The Action also rejected claims 25-27 as being anticipated by Heldin et al., *Nature* (1986) 319:511-514 ("Heldin"). The Action states that "Heldin teaches a PDGF AA homodimer derived from osteosarcoma cells which is disulfide linked." Office Action, page 4. However,

applicants submit that the present claims are not anticipated by Heldin.

In particular, all of the pending claims relate to PDGF A-chain homodimer preparations produced recombinantly in nonhuman cells. Thus, the preparations are free of other human proteins. Heldin, however, isolates a growth factor from human osteosarcoma cells using conventional protein chemistry techniques. Such techniques would inherently result in a protein preparation that included other human protein contaminants. Thus, a significant advantage gained by producing the proteins recombinantly rather than by isolating PDGF from natural sources, is that preparations can be obtained that are devoid of molecules normally present in cells that naturally produce the protein. Potential viral agents from natural sources are also avoided. Thus, a preparation containing a recombinant protein both distinguishes from, and has significant advantages over, the prior art. Indeed, the Board has recognized that the purity of a preparation can be used to impart patentability over prior art references disclosing heterogeneous mixtures. See, *e.g.*, Ex parte Stern, 13 USPQ2d 1379 (BOPAI 1989). Therefore, the claims are believed to patentably distinguish from the Heldin reference.

## Conclusion

Applicants respectfully submit that the claims define an invention which complies with the requirements of 35 USC §112 and which is novel and nonobvious over the art.

Accordingly, allowance is believed to be in order and an early notification to that effect would be appreciated.

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